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Use of mobile devices and the internet for multimedia informed consent delivery and data entry in a pediatric asthma trial: Study design and rationale ☆

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ABSTRACT

Introduction: Phase III/IV clinical trials are expensive and time consuming and often suffer from poor enrollment and retention rates. Pediatric trials are particularly difficult because scheduling around the parent, participant and potentially other sibling schedules can be burdensome. We are evaluating using the internet and mobile devices to conduct the consent process and study visits in a streamlined pediatric asthma trial. Our hypothesis is that these study processes will be non-inferior and will be less expensive compared to a traditional pediatric asthma trial.
Materials/methods: Parents and participants, aged 12 through 17 years, complete the informed consent process by viewing a multi-media website containing a consent video and study material in the streamlined trial. Participants are provided an iPad with WiFi and EasyOne spirometer for use during FaceTime visits and online twice daily symptom reporting during an 8-week run-in followed by a 12-week study period. Outcomes are compared with participants completing a similarly designed traditional trial comparing the same treatments within the same pediatric health-system. After 8 weeks of open-label Advair 250/50 twice daily, participants in both trial types are randomized to Advair 250/50, Flovent 250, or Advair 100/50 given 1 inhalation twice daily. Study staff track time spent to determine study costs.
Results: Participants have been enrolled in the streamlined and traditional trials and recruitment is ongoing.
Conclusions: This project will provide important information on both clinical and economic outcomes for a novel method of conducting clinical trials. The results will be broadly applicable to trials of other diseases.

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1. Introduction

Clinical trials are the cornerstone of research evaluating drug efficacy and safety. Participation in most clinical research studies involves three primary components: providing informed consent; attending visits at the study center; and completing some procedures at home. However, increases in the numbers of procedures, study staff work burden, and longer trial duration coupled with reduced enrollment and retention rate of patient volunteers are increasing the cost and decreasing the value of clinical trials [1]. The cost of Phase III/IV trials was estimated at $47,000 per participant in 2011, an 83% increase from the previous 3 years [2,3] suggesting that the current model for clinical research is fiscally unsustainable.

Current methods of obtaining informed consent using a written document are insufficient [4–11]. Data show that research participants have a poor understanding of the basic elements of informed consent whether provided in oral or written format [4,8,12–17]. Multimedia formats can enhance comprehension in the research informed consent process [5,18] and participants, including children, prefer multimedia to written formats [18,19].

The number of clinic visit procedures, including the number of extraneous procedures, and length of trials have increased while enrollment and retention rates have decreased substantially in recent years [20,21]. Participants often perceive joining a trial as inconvenient and time-consuming [22–25]. Telemedicine has been incorporated into asthma trials since 2001 and well-designed studies indicate mostly positive effects of the intervention [26]. However, no telemedicine trials in asthma have evaluated whether these strategies reduce clinical trials costs [27].

Heath information technologies have been used since the early 2000s to collect data from participants at home and the most common uses in asthma include symptom data, spirometry or peak flow data, and monitoring medication adherence [28–41]. Patients with asthma are enthusiastic about using mobile, internet or electronic means for recording data [39,41–44]. Several studies have evaluated the quality and reliability of the data entered electronically and suggest that information may be more complete and accurate than data entered on written questionnaires [35,36,39].

In 2011, the National Institutes of Health (NIH) issued a Funding Opportunity Announcement entitled "Pilot Studies to Develop and Test Novel, Low-Cost Methods for the Conduct of Clinical Trials (RFA-HL-12-019)". The goals for the application were to test new and innovative designs that have not been previously studied but that hold potential for increased efficiency and reduced cost of conducting clinical trials. Emphasis was to be placed on exploring novel methods for obtaining consent, reducing specialized infrastructure, minimizing visits, developing low-cost methods for monitoring study conduct, and testing the feasibility in a clinical trial.

These features have been incorporated into the Use of *M*obile Devices and the *I*nternet to Streamline an Asthma *C*linical *T*rial (MICT) grant that will compare a *streamlined* design with a *traditional* clinical trial for pediatric asthma funded by the NIH (R01HL114899) and be conducted at outpatient clinics in the Nemours Children's Health System located in Florida and the Delaware Valley. The purpose of this manuscript is to describe the methods and rationale for the *streamlined* trial.

2. Material and methods

2.1. Trial design

The *traditional* trial is a multi-center, double-blinded, placebo-controlled study designed to determine the optimal way to de-escalate therapy in patients with moderate persistent asthma that is well controlled on a fixed-dose combination of inhaled corticosteroid plus a long-acting beta$_2$-agonist (Long-acting Beta Agonist Step Down Study [LASST, NCT01437995]). The trial is being conducted at 18 academic asthma research centers that are part of the American Lung Association Asthma Clinical Research Centers (ALA-ACRC) network. GlaxoSmithKline (GSK) provided funding and blinded drug for the trial but did not have input into the scientific design. The trial was conceived and designed by academic researchers of the ALA-ACRC.

The *streamlined* trial [MICT, NCT02061280] is modeled after the *traditional* trial. While the *traditional* is being conducted at all of the 18 ALA-ACRC academic sites including the Nemours Children's Health System sites in Jacksonville FL, Orlando FL, and Wilmington DE, the *streamlined* trial is being conducted only at Nemours Children's Health System sites (Jacksonville FL, Orlando FL, Pensacola FL, Wilmington DE, and Philadelphia PA). GSK had no input into the concept, design, or implementation of the *streamlined* trial. Researchers from the Nemours Children's Health System and the ALA-ACRC Data Coordinating Center were responsible for the design of the *streamlined* trial.

The relationship between the trial designs for the *streamlined* and *traditional* trials is shown in Figs. 1 and 2.

The specific aims of MICT are: to measure and compare consent comprehension using web-based delivery of informed consent material via a dynamic interactive multimedia platform (Aim 1); to compare timeliness and completeness of study questionnaire and diary data completed electronically using an iPad with wireless internet access, and quality of spirometry performed during FaceTime visits with study staff observing participants who are using an EasyOne Plus meter from their home (Aim 2); and to compare Asthma Control Test scores between the *streamlined* and *traditional* trial design in order to test whether employing the novel internet and mobile device methods in the *streamlined* approach alter the clinical trial's clinically based outcomes (Aim 3). The outcomes for each aim will be compared with a concurrently conducted *traditional* clinical trial (LASST) also performed within the Nemours Children's Health System.

The primary differences between the *traditional* trial and the *streamlined* trial are listed in Table 1.

The shortened duration and smaller sample size of the *streamlined* study are due to the pilot nature of the grant. The *streamlined* trial is performed only in adolescents because the study is being conducted within a pediatric health-system that is only enrolling adolescents into the *traditional* trial. The consent processes differ because Aim 1 is to evaluate a novel method for obtaining informed consent (described below). Study treatments are open-label in the *streamlined* trial due to the unavailability of blinded drug from GSK. The Asthma